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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,121	10/20/2000	Jeffrey Schlom	45394	7805

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DAVID S. RESNICK
NIXON PEABODY LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/693,121	SCHLOM ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29* is/are pending in the application.

4a) Of the above claim(s) *21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-20,22 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed 1/02/2003 (paper no 9) is acknowledged and entered into the record. Accordingly, claims 18 and 29 are amended.

2. Currently, claims 17-29 are pending, claims 21 and 23 are withdrawn from further prosecution as being drawn to a non-elected subject matter. Applcaint is reminded to cancel all non-elected claims.

3. Therefore, claims 17-20, 22, and 24-29 are examined on the record.

Information Disclosure Statement

4. The Information Disclosure Statement filed 3/1/2001 (paper no. 4) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claims Objections Withdrawn

5. The objection of claim 18 is withdrawn in view of the amendment to the claim.

Claim Rejections Withdrawn - 35 USC § 112, 2nd paragraph

6. The rejection of claim 29 under 35 USC 112, 2nd paragraph as being indefinite is withdrawn in view of the amendments to the claims.

Claim Rejections Withdrawn – Double Patenting

7. The rejection of claims 17-20, 22, and 24-25 under 35 USC 101 Double Patenting is withdrawn in view of the persuasive arguments set forth by the applicant.

Claim Rejections Withdrawn - 35 USC § 102

8. The rejection of claims 17 and 26 under 35 USC 102(b) as being anticipated by Bronte *et al* is withdrawn in view of the persuasive arguments set forth by the applicant.

Claim Rejections Withdrawn - 35 USC § 103

9. The rejection of claims 17-20,22, and 24-25 under 35 USC 103(a) as being obvious over Bronte *et al* in view of Correale *et al* is withdrawn in view of the arguments set forth by the applicant.

Claim Rejections Maintained - 35 USC § 112, 2nd paragraph

10. The rejection of claims 17-20, 22, 24-28 under 35 USC 112, 2nd paragraph is maintained for the reasons of record.

11. With regard to claim 17 in the recitation of the terms "sufficient" and "effective amounts", applicant argues that the specification provides ample description of the term and that the term is to be read in the context of an amount that is able to stimulate. Applicant's arguments have been carefully considered but are not found persuasive for the following reason. The amount that is added when in enough quantity can be effective in generating an immune response. Because there is no indication in the specification that would provide one of skill in the art with the minimum and or maximum amounts, one of skill in the art would not know the metes and bounds of the term.

12. With regard to claims 18 and 19 in the recitation of the term "additional", applicant argues that the purpose of the "additional PSA" is to act as a booster, however, this limitation is not present in the claims and as currently interpreted, the "additional PSA" can read on other amounts that may not act as booster doses.

13. With regard to claims 17-20,22, and 24-28 in the recitation of the term "T-cell eliciting epitope thereof", applicant argues that the specification provides examples of useful PSA epitopes that can be used to elicit an immune response. Applicant's

arguments were carefully considered but are not found persuasive because there is still no indication of which epitopes are encompassed by the claims. Any sequence that is greater than 3 amino acids in PSA can be considered an epitope that can elicit an immune response. Because the specification has not clearly defined what the term fully encompasses, the metes and bounds of the term cannot be determined.

NEW GROUNDS OF REJECTON

Claim Rejections - 35 USC § 112, 2nd paragraph

14. Claims 17-20, 22, and 24-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

15. Regarding claims 17 and dependent claims thereof in the recitation of the term "epitope", it is unclear from the specification as to which epitope is encompassed within the scope of the claims. The intended epitope has not been defined.

16. Regarding claims 17 and dependent claims thereof in the recitation of the term "pox virus", it is unclear as to which pox viruses are included within the scope of the claims, does the applicant intended to swine pox?

17. Regarding claims 17-19 and dependent claims thereof in the recitation of the term "contacting", it is to what this would entail. Would the simple act of touching the compound to the skin of a host enable the method to work? Because it is unclear as to what type of administration is intended by the term, the metes and bounds of the term cannot be adequately determined.

Claim Rejections - 35 USC § 112, 1st paragraph

18. Claims 17-20, 22, 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of generating an antibody response by administering to a host an attenuated vaccinia virus , wherein the said vector comprises a PSA gene cloned into the TK region and a gene encoding B7.1 or B7.2 co-stimulatory molecules, IL-2, IL-6, or IL-12 cytokine, does not reasonably provide enablement for a method of generating any and all types of immune responses comprising the contacting of a host with PSA and a cytokine or co-stimulatory molecule, further comprising the contacting of additional PSA and cytokine or co-stimulatory molecule with any and all types of pox viruses. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims of the instant invention are drawn to a method of contacting a host with PSA and a cytokine or co-stimulatory, wherein the PSA and cytokine or co-stimulatory molecule are introduced through a pox virus. The claims are further limited to subsequent additions of PSA and cytokine or co-stimulatory molecules introduced in the same manner. The claims also recite pox viruses selected from the groups consisting of suipox, avipox, capripox, and orthopox.

The art of record teaches that the administration of pox viruses, especially vaccinia viruses (a member of the orthopox family), are modified so as to remove any virulence and to provide a safe and efficacious delivery of tumor associated antigens (TAA). The art also teaches that pox viruses are species specific. One such example of art, Paoletti *et al* (Ann N Y Acad Sci 1993 Aug 12;690:292-300) teaches that the

attenuated vaccinia viruses NYVAC and ALVAC have been modified to reduce the virulence of the virus and to increase host range. Paoleti *et al* also teaches that in the absence of modifications, viruses such as avipox, are ineffective in humans due to premature abortion of DNA replication.

The specification of the instant application discloses the administration to monkeys an attenuated vaccinia virus comprising a gene encoding PSA. The specification also specifically teaches that the immune response generated was primarily an IgM response (see pg 24. line 29). However, nowhere in the specification does it teach of how to use pox viruses in general, wherein the pox virus is in its regular virulent form. There are no limitations within the claims that specifically call for the use of any attenuated virus. It is not clear how a regular pox virus encoding a PSA would be considered effective if administered to a subject because additional immune responses either cellular or humoral responses may prevent and destroy the administered virus. Further, the host may be subject to a systemic infection by the addition of certain viruses. The specification is also deficient in teaching one of skill in the art how to use specie specific pox viruses in subjects such as primates, because it is known and accepted in the art that avipox viral vectors are only effective in avian species. Therefore, the artisan would be forced to determine how the administration of avipox viral vectors to a subject such as a monkey would be considered efficacious. Furthermore, the steps for administration have not been clearly outlines in the specification. The claims recited contacting a host with a PSA. It is not clear from the specification is this "contacting" is a topical ointment comprising a vaccinia virus

encoding a PSA. Because the skilled artisan is unclear as to how this "contacting" is to take place, he would have to experiment with different modes of administration such as oral, subcutaneous or intramuscular injections, and or suppositories.

In addition, the specification is also lacking in the proper disclosure of the effects of adding other cytokines to the system would effect the outcome of generating a proper response to the PSA antigen. It is well known in the art that different cytokines elicit different immune responses. The specification has not taught what effect if any the co-administration of cytokines with PSA would have on the generation of any response or if the co-administration would cause a hyper-immune response causing the subject to be in an elevated immune state. All the instant specification has taught is the effects administering vaccinia virus encoding PSA and the elicitation of a IgM response. Furthermore, different cytokines can elicit different types of TH-1 or TH-2 responses. Because the specification has not taught how to differentiate between the two types of TH responses and because the TH response are used elicited for different reasons, skilled artisan would be forced into a large quantity of experimentation to determine what types of response is generated with the addition of other cytokines. Therefore, the specification is not enabled for the scope of any and all immune response, pox viruses, and the co-administration of cytokines or co-stimulatory molecules for the generation of any and all types of immune response.

Claim Rejections – Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 17-20, 22, and 24-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6,8, and 11-12 of U.S. Patent No. 6,165,460 and Schlom *et al* (WO 92/19266). Claims of the instant invention are drawn to a method of generating an immune response to PSA comprising the contacting of a host with PSA and a cytokine or co-stimulatory molecule. The claims are further limited to the additional administration of PSA and cytokines by way of recombinant expression of a vaccinia virus expressing either PSA or a cytokine. Prior U.S. Patent 6,165,460 claims a method of generating an immune response to PSA comprising the contacting of a host with PSA and subsequently further contacting a host with additional PSA expressed by a vaccinia virus. U.S. Patent 6,165,460 however does not teach the addition of cytokines and co-stimulatory molecules, however, both Schlom *et al* and Hodge *et al* do teach the administration of cytokines and co-stimulatory molecules expressed in vaccinia viruses for the treatment of cancer. Therefore it would have been obvious to combine the references with that of U.S. Patent 6,165,460 because the patent discloses the method of generating an immune response to PSA and further teaches that additional PSA is administered through the

use of a vaccinia virus. The vaccinia virus expressing cytokines and co-stimulatory molecules is also taught for the treatment of cancers and therefore one would be motivated to combine because both have been shown to be used in the treatment of cancers.

Claim Rejections - 35 USC § 103

21. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

22. Claims 17-20, 22, 24-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scholm *et al* (WO 92/19266A1) or Hodge *et al* (Int. J. Cancer 1995;63:231-237) in view of Hodge (Cancer Res 1994 Nov;54(21):5552-5). Claims are drawn to a method of generating an immune response to PSA comprising the contacting of a host with PSA and a cytokine or co-stimulatory molecule.

Scholm *et al* teach a method of generating an immune response to CEA comprising the administration of CEA and a cytokine expressed in a vaccinia virus and show the potent effects of this combination generating an immune response to CEA. However, Scholm *et al* do not specifically teach the generation of an immune response to PSA.

Hodge *et al* (1995) teach the expression of PSA in vaccinia virus and the subsequent administration of PSA to monkeys and the ability of the administered viral vector expressing PSA to generate an immune response. Hodge *et al* further discloses the successful administration of CEA expressed in vaccina viruses for the generation of an immune response against CEA and how little side effects were observed in this

administration. Hodge *et al* (1994) teach the anti-tumor immunity of vaccinia viruses expressing co-stimualtory molecules B7-1 and B7-2 and show that the administration of these co-stimualtory molecules aids in the treatment and anti-tumor effects.

Therefore, it would have been *prima facie* obvious to one of skill in the art at the time the invention was made to generate an immune response to PSA because the art at the time of filing provided all the necessary methods steps and products to accomplish the instant invention. Schlom *et al* provided the necessary method steps of administering CEA expressed in a vaccinia virus to generate an immune response against CEA. In addition, Scholm *et al* also provided the method of further adding cytokines to help in the further elicitation of an immune response to CEA. Hodge *et al* (1995) provided the method of generating an immune response to PSA in monkeys and further alludes to the successful uses of the immune response generation with CEA as taught by Schlom *et al*. Hodge *et al* (1994) provides the applicant's of the instant invention with the usefulness of co-stimulatory molecules which are found to also provide anti-tumor effects when administered by way of vaccinia virus vectors. Therefore, one of ordinary skill in the art at the time of filing had all the necessary motivation to combine the references to arrive at the instant invention because Hodge *et al* provides all the necessary indications of using PSA in place of CEA as taught by Scholm *et al* and further states that the methods proved to be safe with "little side effects" (see page 236). One of skill in the art would have expected a reasonable amount of success in combining the references because Hodge *et al* states that two

other groups have reported successful attempts of this methods with CEA and all showed promise in generating an immune response.

Claim Rejections - 35 USC § 103

23. Claims 17-20, 22, 24-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paoletti *et al* (U.S. Patent 5,833,975) or Hodge *et al* (Int. J. Can. 1995;63:231-237), in view of Hodge *et al* (Cancer Res 1994 Nov;54(21):5552-5). See above rejections for claim limitations. Paoletti *et al* teaches a method of generating an immune response against with a vaccinia virus encoding a TAA and a cytokine. However, Paoletti *et al* do not specifically teach which TAA and do specifically teach the administration of a co-stimulatory molecule.

24. Hodge *et al* (1995) do specifically teach that vaccinia virus encoding a PSA gene can be used as a source to generate an immune response. In addition, Hodge *et al* (1994) specifically teach the administration of vaccinia virus expressing co-stimulaotry molecules.

25. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to generate an immune response against PSA through the administration of a vaccinia virus encoding a PSA gene and a cytokine or co-stimulatory molecule because Paoletti *et al* already taught the general administration technique using a vaccinia virus encoding a TAA and a cytokine and the generation of an immune response to the TAA. It would have been obvious to substitute PSA for the TAA disclosed in the Paoletti *et al* reference because it is well known that PSA is a TAA for prostate cancers. Therefore, the artisan would have been motivated to combine the

references because the basic method of using a vaccinia virus to generate an immune response was already disclosed as being a useful method and the fact that PSA was a known and readily available TAA cold have been easily substituted. The addition or co-administration of cytokines and or co-stimulatory molecules was also taught and known in the art. As a matter of fact, Paoletti *et al* disclosed the co-administration of cytokines, and because Hodge *et al* (1994) taught that the expression of co-stimulatory molecule B7-1 and B7-2 were effective in generating an immune response, the artisan would also be motivated to substitute cytokines with co-stimualtory molecules taught by Hodge *et al* (1994).

Conclusion

No claims are allowed. This action is made NON-FINAL to allow the applicant a chance to respond to the new arguments made in the instant office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
March 24, 2003

ALI R. SALIMI
PRIMARY EXAMINER